

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE  
 in its capacity as elected Office

|                                                                               |                                                                   |
|-------------------------------------------------------------------------------|-------------------------------------------------------------------|
| <b>Date of mailing (day/month/year)</b><br>01 November 2000 (01.11.00)        |                                                                   |
| <b>International application No.</b><br>PCT/US00/08519                        | <b>Applicant's or agent's file reference</b><br>OCR-1001          |
| <b>International filing date (day/month/year)</b><br>30 March 2000 (30.03.00) | <b>Priority date (day/month/year)</b><br>31 March 1999 (31.03.99) |
| <b>Applicant</b><br>CAPPELLO, Michael et al                                   |                                                                   |

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

29 September 2000 (29.09.00)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

|                                                                                                                                          |                                                                                  |
|------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| <b>The International Bureau of WIPO</b><br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br>Facsimile No.: (41-22) 740.14.35 | <b>Authorized officer</b><br>Charlotte ENGER<br>Telephone No.: (41-22) 338.83.38 |
|------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|

# PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

## PCT

To: MARY M. KRINSKY  
79 TRUMBULL STREET  
NEW HAVEN CT 06511-3708

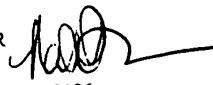
**PTO/PCT Rec'd 25 SEP 2001**

### NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

|                                                        |                                                             |
|--------------------------------------------------------|-------------------------------------------------------------|
| Date of Mailing<br>(day/month/year) <b>05 JUL 2000</b> |                                                             |
| Applicant's or agent's file reference<br>OCR-1001      | FOR FURTHER ACTION See paragraphs 1 and 4 below             |
| International application No.<br>PCT/US00/08519        | International filing date<br>(day/month/year) 30 MARCH 2000 |
| Applicant<br>YALE UNIVERSITY                           |                                                             |

1. ☒ The applicant is hereby notified that the international search report has been established and is transmitted herewith.  
**Filing of amendments and statement under Article 19:**  
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):  
**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.  
**Where?** Directly to the International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35  
 For more detailed instructions, see the notes on the accompanying sheet.
2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3. ☐ With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
  - ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
  - ☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. **Further action(s):** The applicant is reminded of the following:
  - Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 *bis* 1 and 90 *bis* 3, respectively, before the completion of the technical preparations for international publication.
  - Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).
  - Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

|                                                                                                                       |                                                                                                                            |
|-----------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|
| Name and mailing address of the ISA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231 | Authorized officer<br>HOLLY SCHNIZER  |
| Facsimile No. (703) 305-3230                                                                                          | Telephone No. (703) 308-0196                                                                                               |

(See notes on accompanying sheet)

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|                                                   |                                                                                                                                                                                                                                                                                                                            |                                                            |
|---------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| Applicant's or agent's file reference<br>OCR-1001 | <div style="display: flex; justify-content: space-between;"> <div style="width: 30%;"> <b>FOR FURTHER ACTION</b> </div> <div style="width: 70%;">                     see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5                 </div> </div> |                                                            |
| International application No.<br>PCT/US00/08519   | International filing date (day/month/year)<br>30 MARCH 2000                                                                                                                                                                                                                                                                | (Earliest) Priority Date (day/month/year)<br>30 MARCH 1999 |
| Applicant<br>YALE UNIVERSITY                      |                                                                                                                                                                                                                                                                                                                            |                                                            |

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☒ contained in the international application in written form.

☒ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☐ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (See Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. 1

☒ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/08519

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 1/00, 14/00; A61K 38/00

US CL : 514/2, 822; 530/350

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 514/2, 822; 530/350

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Extra Sheet.

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category*     | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                      | Relevant to claim No.              |
|---------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| Y<br>---<br>A | WO 95/12615 A1 (UNIVERSITY OF NOTTINGHAM) 11 May 1995 (11/05/1995), see entire document, especially p. 11, claim 2, p. 12, claim 7, and Figure 4.                                       | 12 and 16-19<br>-----<br>1-20      |
| Y<br>---<br>A | FURMIDGE et al. The anti-haemostatic strategies of the human hookworm <i>Necator americanus</i> . Parasitology. 1995, Vol. 112, pages 81-87, especially page 84, figure 3, and page 86. | 12, 14, and 16-19<br>-----<br>1-20 |

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

\* Special categories of cited documents:

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

14 JUNE 2000

Date of mailing of the international search report

05 JUL 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231  
Facsimile No. (703) 305-3230

Authorized officer

HOLLY SCHNIZER

Telephone No. (703) 308-0196

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/08519

## B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

STN (MEDLINE, BIOSIS, CAPLUS); EAST; search terms: GPIIb/IIIa, GPIa/IIa, fibrinogen, collagen, ancylostoma duodenale, ancylostoma ceylanicum, necator americanus, ancylostoma caninum, hookworm, platelet inhibition, epinephrine, thrombin, ADP, apyrase.

PTO/PCT Rec'd 25 SEP 2001

## PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITYTo:  
MARY M. KRINSKY  
79 TRUMBULL STREET  
NEW HAVEN, CT 06511-3708

PCT

AUG 22 2001  
hul.

WRITTEN OPINION

(PCT Rule 66)

|                                                                                   |                                            |                                     |                                                        |
|-----------------------------------------------------------------------------------|--------------------------------------------|-------------------------------------|--------------------------------------------------------|
| Applicant's or agent's file reference                                             |                                            | Date of Mailing<br>(day/month/year) | 20 AUG 2001                                            |
| OCR-1001                                                                          |                                            | REPLY DUE                           | within 1 months/days from<br>the above date of mailing |
| International application No.                                                     | International filing date (day/month/year) | Priority date (day/month/year)      |                                                        |
| PCT/US00/08519                                                                    | 30 March 2000 (30.03.2000)                 | 31 March 1999 (31.03.1999)          |                                                        |
| International Patent Classification (IPC) or both national classification and IPC |                                            |                                     |                                                        |
| IPC(7): C07K 1/00, 14/00; A61K 38/00 and US Cl.: 514/2, 822; 530/350              |                                            |                                     |                                                        |
| Applicant                                                                         |                                            |                                     |                                                        |
| YALE UNIVERSITY                                                                   |                                            |                                     |                                                        |

- This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.
- This opinion contains indications relating to the following items:

- ☒ Basis of the opinion
- ☐ Priority
- ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Lack of unity of invention
- ☒ Reasoned statement under Rule 66.2 (a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Certain documents cited
- ☐ Certain defects in the international application
- ☐ Certain observations on the international application

- The applicant is hereby **invited to reply** to this opinion.

**When?** See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension. See rule 66.2(d).~~

**How?** By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also** For an additional opportunity to submit amendments, see Rule 66.4.  
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.  
For an informal communication with the examiner, see Rule 66.6

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

- The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 30 July 2001 (30.07.2001).

Name and mailing address of the IPEA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231  
Facsimile No. (703)305-3230

Authorized officer

Stephen Tu

Telephone No. 703-305-3150

TERRY J. DEY  
PARALEGAL SPECIALIST  
TECHNOLOGY CENTER 1600

WRITTEN OPINION

International application No.

PCT/US00/08519

I. Basis of the opinion

1. With regard to the elements of the international application:\*

- ☒ the international application as originally filed
- ☒ the description:  
 pages 1-25, as originally filed  
 pages NONE, filed with the demand  
 pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the claims:  
 pages 26 and 27, as originally filed  
 pages NONE, as amended (together with any statement) under Article 19  
 pages NONE, filed with the demand  
 pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the drawings:  
 pages 1-5, as originally filed  
 pages NONE, filed with the demand  
 pages NONE, filed with the letter of \_\_\_\_\_
- ☒ the sequence listing part of the description:  
 pages 1-2, as originally filed  
 pages NONE, filed with the demand  
 pages NONE, filed with the letter of \_\_\_\_\_

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

- ☒ contained in the international application in printed form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE \_\_\_\_\_
- ☐ the claims, Nos. NONE \_\_\_\_\_
- ☐ the drawings, sheets/fig NONE \_\_\_\_\_

5. ☐ This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed."

# WRITTEN OPINION

International application No.  
PCT/US00/08519

## V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. STATEMENT

|                               |                                |     |
|-------------------------------|--------------------------------|-----|
| Novelty (N)                   | Claims <u>1-20</u>             | YES |
|                               | Claims <u>NONE</u>             | NO  |
| Inventive Step (IS)           | Claims <u>1-11, 13, 15, 20</u> | YES |
|                               | Claims <u>12, 14, 16-19</u>    | NO  |
| Industrial Applicability (IA) | Claims <u>1-20</u>             | YES |
|                               | Claims <u>NONE</u>             | NO  |

### 2. CITATIONS AND EXPLANATIONS

Claims 1-20 meet the criteria for novelty under PCT Article 33(2), because the prior art does not disclose the polypeptide of SEQ ID NO:2 or methods of treatment to inhibit platelet function utilizing the polypeptide, as claimed by Applicants.

Claims 1-11, 13, 15, and 20 meet the criteria for novelty under PCT Article 33(3), because the prior art does not teach the polypeptide of SEQ ID NO:2 or methods of treatment to inhibit platelet function utilizing the polypeptide, as set forth in these claims.

Claims 12, 14, and 16-19 lack an inventive step under PCT Article 33(3) as being obvious over PRITCHARD et al., WO95/12615 in view of FURMIDGE et al., (Parasitology (1995) 112: 81-87). PRITCHARD et al. teaches the pharmaceutical use of derivatives of excretory-secretory (ES) products of *Necator americanus*, particularly as an inhibitor of platelet aggregation. However the reference does not teach or suggest mechanism by which these proteins inhibit platelet aggregation. FURMIDGE et al. teaches mechanisms by which the ES products of *N. Americanus* inhibit platelet aggregation. Specifically, the references indicate that the proteins interfere with the interaction of fibrinogen with platelet  $\alpha\text{IIb}\beta_3$ , which Applicant has referred to as GPIIb/IIIa.

Claims 1-20 meet the criteria for industrial applicability as defined by PCT Article 33(4).

----- NEW CITATIONS -----  
NONE



WRITTEN OPINION

International application No.  
PCT/US00/08519

Supplemental Box  
(To be used when the space in any of the preceding boxes is not sufficient)

TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

091937555

## PATENT COOPERATION TREATY

## PCT

REC'D 15 MAR 2002

WIPO PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                               |                                |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Applicant's or agent's file reference                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |                                |
| OCR-1001                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | International filing date (day/month/year)                                                                                    | Priority date (day/month/year) |
| International application No.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | 30 March 2000 (30.03.2000)                                                                                                    | 31 March 1999 (31.03.1999)     |
| PCT/US00/08519                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | International Patent Classification (IPC) or national classification and IPC                                                  |                                |
| IPC(7): C07K 1/00, 14/00; A61K 38/00 and US Cl.: 514/2, 822; 530/350                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                               |                                |
| Applicant                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                               |                                |
| YALE UNIVERSITY                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                                                                               |                                |
| <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>3</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u>0</u> sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"><li>I <input checked="" type="checkbox"/> Basis of the report</li><li>II <input type="checkbox"/> Priority</li><li>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</li><li>IV <input type="checkbox"/> Lack of unity of invention</li><li>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li><li>VI <input type="checkbox"/> Certain documents cited</li><li>VII <input type="checkbox"/> Certain defects in the international application</li><li>VIII <input type="checkbox"/> Certain observations on the international application</li></ul> |                                                                                                                               |                                |
| Date of submission of the demand                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Date of completion of this report                                                                                             |                                |
| 29 September 2000 (29.09.2000)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 26 February 2002 (26.02.2002)                                                                                                 |                                |
| Name and mailing address of the IPEA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        | Authorized Officer<br>Chin-Min Kun                                                                                            |                                |
| Facsimile No. (703) 305-3230                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | Telephone No. (703) 308-0196                                                                                                  |                                |

Form PCT/IPEA:409 (cover sheet/July 1998)

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US00/08519

**I. Basis of the report**1. With regard to the **elements** of the international application:\*

- ☒ the international application as originally filed.
- ☒ the description:  
pages 1-25 as originally filed  
pages NONE filed with the demand  
pages NONE filed with the letter of \_\_\_\_\_.
- ☒ the claims:  
pages 26 and 27 as originally filed  
pages NONE as amended (together with any statement) under Article 19  
pages NONE filed with the demand  
pages NONE filed with the letter of \_\_\_\_\_.
- ☒ the drawings:  
pages 1-5 as originally filed  
pages NONE filed with the demand  
pages NONE filed with the letter of \_\_\_\_\_.
- ☒ the sequence listing part of the description:  
pages 1-2 as originally filed  
pages NONE filed with the demand  
pages NONE filed with the letter of \_\_\_\_\_.

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.  
These elements were available or furnished to this Authority in the following language \_\_\_\_\_ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☒ contained in the international application in printed form.
- ☒ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages NONE
- ☒ the claims, Nos. NONE
- ☒ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\*

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/US00/08519

## V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. STATEMENT

Novelty (N)

Claims 1-20

YES

Claims NONE

NO

Inventive Step (IS)

Claims 1-11, 13, 15 and 20

YES

Claims 12, 14, 16-19

NO

Industrial Applicability (IA)

Claims 1-20

YES

Claims NONE

NO

### 2. CITATIONS AND EXPLANATIONS

Claims 1-20 meet the criteria for novelty under PCT Article 33(2), because the prior art does not disclose the polypeptide of SEQ ID NO:2 or methods of treatment to inhibit platelet function utilizing the polypeptide, as claimed by Applicants.


Claims 1-11, 13, 15 and 20 meet the criteria for novelty under PCT Article 33(3), because the prior art does not teach the polypeptide of SEQ ID NO:2 or methods of treatment to inhibit platelet function utilizing the polypeptide, as set forth in these claims.

Claims 12, 14 and 16-19 lack an inventive step under PCT Article 33(3) as being obvious over PRITCHARD et al. (WO 95/12615) in view of FURMIDGE et al. (Parasitology (1995) 112:81-87). PRITCHARD et al. teach the pharmaceutical use of derivatives of excretory-secretory(ES) products of *Necator americanus*, particularly as an inhibitor of platelet aggregation. However, the reference does not teach or suggest mechanism by which these proteins inhibit platelet aggregation. FURMIDGE et al. teach mechanisms by which the ES products of *N. americanus* inhibit platelet aggregation. Specifically, the references indicate that the proteins interfere with the interaction of fibrinogen with platelet aIIbB3, which Applicant has referred to as GPIIb/IIIa.

Claims 1-20 meet the criteria for industrial applicability as defined by PCT Article 33(4).

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US00/08519

| <b>A. CLASSIFICATION OF SUBJECT MATTER</b><br>IPC(7) :C07K 1/00, 14/00; A61K 38/00<br>US CL :514/2, 822; 530/350<br>According to International Patent Classification (IPC) or to both national classification and IPC                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                  |                                                                                                                                                            |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
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| <b>B. FIELDS SEARCHED</b><br>Minimum documentation searched (classification system followed by classification symbols)<br>U.S. : 514/2, 822; 530/350<br><br>Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched<br><br>Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)<br>Please See Extra Sheet.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |                                                                                                                                                                                                                                                  |                                                                                                                                                            |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| <b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                  |                                                                                                                                                            |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| Category*                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                               | Relevant to claim No.                                                                                                                                      |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| Y<br>---<br>A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | WO 95/12615 A1 (UNIVERSITY OF NOTTINGHAM) 11 May 1995 (11/05/1995), see entire document, especially p. 11, claim 2, p. 12, claim 7, and Figure 4.                                                                                                | 12 and 16-19<br>-----<br>1-20                                                                                                                              |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| Y<br>---<br>A                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             | FURMIDGE et al. The anti-haemostatic strategies of the human hookworm <i>Necator americanus</i> . Parasitology. 1995, Vol. 112, pages 81-87, especially page 84, figure 3, and page 86.                                                          | 12, 14, and 16-19<br>-----<br>1-20                                                                                                                         |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| <input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> See patent family annex.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                  |                                                                                                                                                            |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| <table border="0"><tr><td>* Special categories of cited documents:</td><td>*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</td></tr><tr><td>*A* document defining the general state of the art which is not considered to be of particular relevance</td><td>*X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</td></tr><tr><td>*E* earlier document published on or after the international filing date</td><td>*Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art</td></tr><tr><td>*L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</td><td>*G* document member of the same patent family</td></tr><tr><td>*O* document referring to an oral disclosure, use, exhibition or other means</td><td></td></tr><tr><td>*P* document published prior to the international filing date but later than the priority date claimed</td><td></td></tr></table> |                                                                                                                                                                                                                                                  |                                                                                                                                                            | * Special categories of cited documents: | *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention | *A* document defining the general state of the art which is not considered to be of particular relevance | *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone | *E* earlier document published on or after the international filing date | *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art | *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | *G* document member of the same patent family | *O* document referring to an oral disclosure, use, exhibition or other means |  | *P* document published prior to the international filing date but later than the priority date claimed |  |
| * Special categories of cited documents:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention                                              |                                                                                                                                                            |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| *A* document defining the general state of the art which is not considered to be of particular relevance                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone                                                                     |                                                                                                                                                            |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| *E* earlier document published on or after the international filing date                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |                                                                                                                                                            |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | *G* document member of the same patent family                                                                                                                                                                                                    |                                                                                                                                                            |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| *O* document referring to an oral disclosure, use, exhibition or other means                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                  |                                                                                                                                                            |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| *P* document published prior to the international filing date but later than the priority date claimed                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |                                                                                                                                                                                                                                                  |                                                                                                                                                            |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| Date of the actual completion of the international search<br>14 JUNE 2000                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |                                                                                                                                                                                                                                                  | Date of mailing of the international search report<br>05 JUL 2000                                                                                          |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |
| Name and mailing address of the ISA/US<br>Commissioner of Patents and Trademarks<br>Box PCT<br>Washington, D.C. 20231<br>Facsimile No. (703) 305-3230                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                                                                                                                                  | Authorized officer<br>HOLLY SCHNIZER <br>Telephone No. (703) 308-0196 |                                          |                                                                                                                                                                                                     |                                                                                                          |                                                                                                                                                                              |                                                                          |                                                                                                                                                                                                                                                  |                                                                                                                                                                         |                                               |                                                                              |  |                                                                                                        |  |

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US00/08519

### B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

STN (MEDLINE, BIOSIS, CAPLUS); EAST; search terms: GPIIb/IIIa, GPIa/IIa, fibrinogen, collagen, ancylostoma duodenale, ancylostoma ceylanicum, necator americanus, ancylostoma caninum, hookworm, platelet inhibition, epinephrine, thrombin, ADP, apyrase.